

**Conclusions:** Despite the high degree of sequence homology to *ALS5*, the *ALS6* and *ALS7* genes of *C. albicans* do not mediate adherence to fibronectin. These functional differences despite sequence homology have allowed us to produce chimeric *ALS* genes, and thereby localize the fibronectin-binding domain of *ALS5* to the N-terminal portion of the gene product. This technique will be invaluable in further defining the key binding domain of the *Als5* protein, a critical initial step in the development of novel therapeutics targeted at the inhibition of candidal adherence.

#### **A case report of *Geotrichum* infection in a patient with CLL**

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*Geotrichum* is a ubiquitous fungus distinctive for arthroconidia and septated hyphae. It is present in soil, fruits and dairy products and is a markedly rare human systemic pathogen with a reported mortality rate of 70–75%. We present a neutropenic 64-year male patient with CLL treated since mid 2001 with fludarabine based chemotherapy and prophylactic tmp/smz who was re-admitted for fungemia in February 2002.

The patient's complex illness included four cycles of chemotherapy, and hospitalizations the prior September and December for neutropenic fever with an absolute neutrophil count (ANC) less than 200 on both admissions. During the December admission a biopsy of a left thigh lesion grew *Nocardia brasiliensis* that was treated with appropriate intravenous and then outpatient oral therapy. In January 2002, complaining on this occasion of right lower leg swelling and pain, the patient was readmitted with an ANC of zero. Chemotherapeutic coverage for *Nocardia* was intensified and robust antibiotic management for neutropenia administered. After more than a fortnight of inpatient management, the patient was afebrile and was discharged on outpatient antibiotics. Within two days of discharge, the lab reported fungemia.

On prompt readmission intensive antibacterial and antifungal therapy was given. One-day post admission the blood culture isolate was identified as *Geotrichum*. Imaging revealed multiple lesions in the soft tissues and musculature of both legs. A cystic area of the right lower leg was débrided twice and grew *Geotrichum* on each occasion. A literature search found some relevant papers. A 12-year survey of unusual fungal infections at M D Anderson cancer center reported 2 patients with *Geotrichum* infections. Neither patient survived. A 10-year survey at a tertiary hospital in Bergamo, Italy

identified 3 cases of *Geotrichum* with no survivors. One antifungal sensitivity study reported MIC's for amphotericin B of 0.39 at 50% and 0.78 at 90% while another study reported voriconazole MIC's of 0.20 at 50% and 0.39 at 90%. Our patient's initial antifungal therapy of Abelcet and itraconazole was changed to Abelcet, caspofungin and voriconazole and was later modified to AmBisome, caspofungin, voriconazole and flucy-tosine. Neutrophil production was stimulated with G-CSF and then, based on a published 3 patient case series report, with GM-CSF. Blood cultures have become sterile, but the patient has shown little clinical progress. The *Geotrichum* isolate has been forwarded to research labs for further testing against comprehensive panels of antifungals including the emerging azoles. Our patient resolutely continues to re-request aggressive treatment for this unusual pathogen. The result of this novel therapy against his dire infection remains in question.

#### **Outcome in central nervous system aspergillosis is improved by clinical suspicion and rapid employment of imaging, surgery and therapy**

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The fatality rate associated with central nervous system (CNS) aspergillosis (Asp) in immunocompromised patients is high and often established by autopsy. We report 2 patients who were rapidly diagnosed and treated for CNS Asp and are longtime survivors. Patient 1, a 19-year-old male, was diagnosed as having bone marrow failure 2 years prior to Ewing's sarcoma, at humerus. He had received TBI, chemotherapy, ATG prior to cord blood transplant. Acute mental status changes led to an MRI showing multiple ring enhancing lesions (MREL). Brain diagnosis (dx) showed *A. fumigatus*. The patient received prolonged amphotericin B & 5-FC and GM-CSF. He is now 40 months from CNS Asp. Imaging, neuro exam, and bone marrow are normal. He attends vocational school. Patient 2, an 11-year-old male with acute lymphoblastic leukemia had 4 weeks of induction therapy when fever and cough led to a CT scan (chest) showing multiple lung nodules. CT scan brain showed MREL. Open lung biopsy and craniotomy with drainage showed Asp, all tissues. He received prolonged amphotericin B lipid complex, 5-FC and modified ALL therapy. Thirty months after dx Asp, imaging and neuro exam are normal; his ALL is in remission. He attends high school. With high clinical suspicion, rapid use of imaging – expeditious employment of surgery, prolonged administration of antifungals and maintaining adequate phagocyte counts, the outcome of CNS Asp can be improved.